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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,533	04/25/2006	Glynn Thomas Faircloth	13566.105012	1346

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EXAMINER	
AUDET, MAURY A	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
09/11/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/531,533	FAIRCLOTH ET AL.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 16-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 16-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/24/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response of 4/2/07 and 6/19/07 are acknowledged. Claims 1 and new claims 16-33 are pending and examined on the merits.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1 as provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 6-47 of copending Application No. 10/492,670 (US 2005/0054555 A1), is maintained for the reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '555 claims are to any kahalalide compound, which the specification may be the 4-methylhexyl derivative (present compound) (para 37), including kits., methods of making, and methods of treating cancer (e.g. breast cancer).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112 1st Scope

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1 and 16-33 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutically acceptable salts of kahalalide F "4-methylhexyl); does not reasonably provide enablement for any prodrug, tautomer, or solvate thereof, is maintained for the reasons of record. Applicant's arguments have been considered but are not deemed persuasive.

The rejection is repeated below for continuity of record:

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

> The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is

proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The instant disclosure fails to meet the enablement requirement for the invention above.

The nature of the invention: The invention is described at the outset.

The state of the prior art and the predictability or lack thereof in the art:

Vippagunta, et al. (Adv. Drug Delivery Rev. (2001), May 2001, 48(1): 3-26), *cited merely by example of known references showing the difficulty with determining e.g. solvates, prodrugs, and tautomers of known compounds (and applied broadly to the general class of the former derivatives, all suffering from the same issue of enablement, just as individual references in the art to each specifically would be)*, teaches that, "The common crystalline forms found for a given drug substance are polymorphs and solvates. Crystalline polymorphs have the same chemical composition, but different internal crystal structures, and therefore, possess different physico-chemical properties." (page 4). "Solvates, also known as pseudopolymorphs, are crystalline solid adducts containing solvent molecules within the crystal structure, ... giving rise to unique differences in the physical and pharmaceutical properties of the drug. If the incorporated solvate is water, a solvate is termed a hydrate." (page 4).

Vippagunta teaches that, "Because different crystalline polymorphs and solvates differ in crystal packing, and/or molecular conformation as well as in lattice energy and entropy, there are usually significant differences in their physical properties, such as density, hardness, tablet ability, refractive index, melting point, enthalpy of fusion, vapor pressure, solubility, dissolution rate, other thermodynamic and kinetic properties and even color. Differences in physical properties of various solid forms have an important effect on the processing of drug substances into drug products, while differences in solubility may have implications on the absorption of the active drug from its dosage form, by affecting the dissolution rate and possibly the mass transport of the molecules." (page 4).

Vippagunta teaches that, "It is very important to control the crystal form of the drug during the various drug development, because any phase change due to polymorph interconversions, desolvation of solvates, formation of hydrates and change in the degree of crystallinity can alter the bioavailability of the drug. When going through a phase transition, a solid drug may undergo a change in its thermodynamic properties, with consequent changes in its dissolution and transport characteristics." (page 5).

Vippagunta teaches that there are reversible and irreversible polymorphs (page 6), and polymorphs which are structural or conformational polymorphs (pages 7-11). Vippagunta further teaches that, "The main challenge in managing the phenomenon of multiple solid forms of a drug is the inability to predict the number of forms that can be expected in a given case." (page 11).

Vippagunta teaches that "Phase changes due to hydration/dehydration and salvation/desolvation of pharmaceutical compounds during processing or in the final product may result in an unstable system that would effect the bioavailability of drug from solid dosage forms. Various types of phase changes are possible in solid-state hydrated or solvated systems in response to changes in environmental conditions... For example, some hydrated compounds may convert to an amorphous phase upon dehydration and some may convert from a lower to a higher state of hydration yielding forms with lower solubility. Alternatively, a kinetically favored but thermodynamically unstable form may be converted during pharmaceutical processing to a more stable and less soluble form." (page 17).

Vippagunta teaches that, "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds... There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates." (page 18).

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification describes (4S) and (4R)-methylhexanoic KF (Examples 1 and 2) as a derivative salt, prodrug, tautomer or solvate, but was not found to provide any other working examples/guidance as to the preparation of such derivatives.

The breadth of the claims and the quantity of experimentation needed: The claims are drawn broadly to the use of any pharmaceutically acceptable salts of kahalalide F "4-methylhexyl) or prodrug, tautomer, or solvate thereof. With the substantial variability among what solvates, prodrugs, and tautomers, can be enably created with the present compound, it would require undue experimentation by one of skill in the art to practice the invention. Absent

sufficient teachings in the specification or art sufficient to overcome the teachings of unpredictability in the art as to enablement of such derivative solvates, prodrugs, and tautomers; it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

II. The rejection of claims 26-33 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the following four (4) cancers in a mammal, based on test data, include: hepatocellular carcinoma (Example 8), human live adenocarcinoma (Example 8), breast cancer (Example 6), and prostate cancer (Example 7), using kahalalide F "4-methylhexyl" or pharmaceutically acceptable salts thereof; does not reasonably provide enablement for treating any cancer, or a viral or fungal infection, is maintained for the reasons of record and based on the state of the art as to enablement of cancer therapy. Applicant's arguments have been considered but are not deemed persuasive.

The rejection is repeated below for continuity of record:

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states is stated above, in the 1st 112 1st rejection,

The instant disclosure fails to meet the enablement requirement for the invention above.

The nature of the invention: The invention is described at the outset.

The state of the prior art and the predictability or lack thereof in the art:

Screening potential anticancer drugs sounds easy. Just take a candidate drug, add it to a tumor type of choice, and then monitor whether the agent kills the cells or inhibits cancer growth. Too bad it hasn't been that simple. Even as investigators try to develop a new generation of more effective and less toxic anticancer drugs that directly target the gene changes propelling cells toward uncontrollable division [], they face a long-standing problem: sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile. (emphasis added) (Gura, p. 1041, . 1).

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification describes treating *in vivo* or *in vitro* cancer cell lines from hepatocellular carcinoma (Example 8), human live adenocarcinoma (Example 8), breast cancer (Example 6), and prostate cancer (Example 7), using kahalalide F "4-methylhexyl" or pharmaceutically acceptable salts thereof. No other forms of cancer were described as being treated or treatable either *in vivo* or *in vitro.*

The breadth of the claims and the quantity of experimentation needed: The claims are drawn broadly to treating any cancer, or viral or fungal infection using kahalalide F "4-methylhexyl" or pharmaceutically acceptable salts thereof. With the substantial variability among what peptides or other compounds are enabled to treat tumors/cancer *in vitro* or *in vivo*, the present specification is not enabled for this breadth. Absent sufficient teachings in the specification or art sufficient to overcome the teachings of unpredictability in the art as to enablement of the invention; it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Observation

As to treating any of the forms of cancer, as well as the 4 noted above, the Examiner also wishes to have Applicant consider that range or amount which is deemed enabled as to "therapeutically effective amount". Although this was not deemed to rise to the level of indefiniteness, Applicant is asked to more distinctly claim this limitation should a definition/support thereto be present in the specification.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 8/20/2007

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Technology Center 1600